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ANTIOXIDANTS AND THEIR ROLL IN HUMAN HEALTH: A REVIEW

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ABSTRACT

Antioxidants are free radical molecules capable of inhibiting the oxidation of other molecules. Antioxidants play an important role to prevent some chronic diseases and protect the health of the individual by their ingestion with the food. Different types of antioxidants are available at present viz., dietary antioxidants, synthetic antioxidants, natural antioxidants, endogenous antioxidants and exogenous antioxidants. Antioxidants protect against damage induced by free radicals and oxidative stress. Antioxidants also act as reducing agents. Antioxidants are available in most of the plant based foods like fruits and vegetables, nuts, oilseeds and also in the form of certain nutrients like vitamin C, vitamin E etc.

KEYWORDS: Antioxidants, Diseases, Free Radicals & Food

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INTRODUCTION

Oxygen is an indispensable element for life. Oxygen is a highly reactive atom that is capable of becoming part of potentially damaging molecules commonly called “free radicals.” Free radicals have tendency of attacking the healthy cells of the body, causing them to lose their structure and function (**Verma and Misra, 2014**). Oxidative stress occurs when the generation of free radicals and active intermediates in a system exceeds the system’s ability to neutralize and eliminate them **(Sies, 1985).** An antioxidant is a molecule capable of inhibiting the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons from a substance to an oxidizing agent **(Rojita and** Satpal, **2011).** Antioxidants are an inhibitor of the process of oxidation, even at relatively small concentration and they have diverse physiological role in the body **(Sunil, 2014).** Oxidative stress plays a major part in the development of chronic and degenerative ailments such as cancer, arthritis, aging, autoimmune disorders, cardiovascular and neurodegenerative diseases **(Lien *et al.*, 2008).** Antioxidants act as reducing agents that prevent oxidative reactions, often by scavenging reactive oxygen species before they damage the cells **(Wolf, 2005).** They are important in prevention of plants pollution damage, disease prevention in both plants and animals and play an important role in the body defense system **(Ahmed and Beigh, 2009).**

History of Anti-Oxidants

Antioxidants have been used for the first time in the nineteenth century in the rubber industry, when it was observed that some molecules identified empirically, could slow the degradation and allow optimization of the process of vulcanization. In the twentieth century antioxidants are then entered in the arsenal of the emerging food industry, as a key tool to curb the oxidative degradation of stored food (**Sunil, 2014**). Early research on the role of antioxidants in biology focused on their use in preventing the oxidation of unsaturated fats, which is the cause of rancidity (**German, 1999).** Antioxidant activity could be measured simply by placing the fat in a closed container

with oxygen and measuring the rate of oxygen consumption.

Antioxidants Classification

Antioxidants in food are classified as viz. dietary antioxidants, synthetic antioxidants, natural antioxidants, endogenous antioxidants and exogenous antioxidants which play an important role in preservation of food **(Anuj *et al.*, 2016).**

Dietary Antioxidants

The dietary antioxidants such as ascorbates, tocopherols and carotenoids are well known and there is a surplus of publications related to their role in health **(Boskou *et al.*, 2005).** Vitamin C, vitamin E, and beta carotene, Beta carotene and other carotenoids and oxycarotenoids, e.g., lycopene and luteinare among the most widely studied dietary antioxidants. Flavonoids have been demonstrated to have anti-inflammatory, antiallergenic, anti-viral, anti-aging, and anti-carcinogenic activity (**Cody *et al.*, 1986).** Fruits and vegetables are major sources of vitamin C and carotenoids, while whole grains and high quality, properly extracted and protected vegetable oils are major sources of vitamin E **(Mark, 1998).**

Synthetic Antioxidant

Synthetic antioxidants are chemically synthesized since they do not occur in nature and are added to food as preservatives to help prevent lipid oxidation **(Shahidi *et al.*, 1992).** Synthetic antioxidants are phenolic compounds such as butylated hydroxyanisol (BHA), butylated hydroxytoluene (BHT), tertiary butyl hydroquinone (TBHQ) and propyl gallate (PG) mostly used in industry. They are mostly used in the food industry because of their effectiveness and being cheaper. They are toxic and have carcinogenic potential which led to the need for natural alternatives **(Thompson and Trush, 1988a, 1988b; Thompson and Moldeus, 1988).** Since about 1980, natural antioxidants have appeared as a healthier and safer alternative to synthetic antioxidants **(Yanishlieva *et al* 2001).**

Natural Antioxidant

Natural antioxidants are found in almost all plants, microorganisms, fungi, and even in animal tissues **(Pokorny *et al.*, 2001).** Natural antioxidants are those oxidants that are found in natural sources, such as fruits, vegetables and meats. There are several common natural antioxidants which are found in everyday foods, the most common of which being Vitamin C (ascorbic acid), Vitamin E (tocopherols), Vitamin A (carotenoids), various polyphenols including Flavonoids, and Anthocyanins (a type of flavonoid), Lycopene (a type of carotenoid), and Coenzyme Q 10, also known as Ubiquitin, which is a type of protein. **(Anuj *et al.*, 2016).** The beneficial effects of consuming plant food are associated with lowering the risk of most cardiovascular diseases and cancer, among other degenerative diseases of aging (**Cuppett *et al.*, 1997).**

Endogenous Antioxidants

In addition to dietary antioxidants, the body relies on several endogenous defense mechanisms to help protect against free radical-induced cell damage. The antioxidant enzymes – glutathione peroxidase, catalase, and superoxide dismutase (SOD) – metabolize oxidative toxic intermediates and require micronutrient cofactors such as selenium, iron, copper, zinc and manganese for optimum catalytic activity. It has been suggested that an inadequate dietary intake of these trace minerals may compromise the effectiveness of these antioxidant defense mechanisms **(Duthie and Brown 1994; Suneel, 2014; Anuj, 2016).** Research indicates that consumption and absorption of these important trace minerals may decrease with aging**. (Duthie and Brown, 1994)**

Exogenous Antioxidants

Exogenous antioxidants can derive from natural sources (vitamins, flavonoids, anthocyanins, some mineral compounds), but can also be synthetic compounds, like butylated hydroxyanisole, butylated hydroxytoluene (**Litescu *et al.*, 2011).** There is an increasing interest in antioxidants, particularly in those intended to prevent the presumed deleterious effects of free radicals in the human body, as well as the deterioration of fats and other constituents of foodstuffs **(Molyneux (2004; Anuj *et al.*, 2008).**

SOURCES AND FUNCTIONS OF ANTIOXIDANTS

Vitamin E

Vitamin E is a fat-soluble vitamin with high antioxidant potency. Vitamin E is one of the most important lipid-soluble primary defense antioxidant (**Abdalla, 2009).** Vitamin E is a most effective chain-breaking antioxidant **(Bashir *et al*., 2004).** Its antioxidant function mainly resides in the protection against lipid peroxidation. Vitamin E has been proposed for the prevention against colon, prostate and breast cancers, some cardiovascular diseases, ischemia, cataract, arthritis and certain neurological disorders **(Mayo Clinic Medical Information, 2005).** The dietary sources of vitamin E are vegetable oils, wheat germ oil, whole grains, nuts, cereals, fruits, eggs, poultry and meat. Cooking and storage may destroy natural d- α-tocopherol in foods **(Willcox *et al.*, 2004).**

Vitamin C

Vitamin C also known as ascorbic acid, it is a water-soluble vitamin. Health benefits of vitamin C are antioxidant, anti-atherogenic, anti-carcinogenic, immunomodulator. Functions of Vitamin C are with Vitamin C intake is inversely related to cancer, with protective effects shown for cancer of the lung, breast, pancreas, stomach, cervix, rectum and oral cavity **(Simon *et al.*, 2001).** Natural sources of vitamin C are acid fruits, green vegetables and tomatoes. Ascorbic acid is a labile molecule; therefore it may be lost from during cooking **(Naidu., 2003).**

Beta-Carotene

Beta-carotene has antioxidant properties that can help neutralize free radicals – reactive oxygen molecules potentially damaging lipids in cell membranes and genetic material, which may lead to the development of cardiovascular disease and cancer **(Pavia and Russell, 1999).** It is consider as a strong antioxidant and the best quencher of singlet oxygen. Beta-carotene is a fat soluble member of the carotenoids which are considered provitamins because they can be converted to active vitamin A. Beta-carotene is present in many fruits, grains, oil and vegetables (carrots, green plants, squash, spinach) **(Willcox *et al*., 2004).** In vitro studies indicate that carotenoids can also inhibit the oxidation of fats under certain conditions. They may have anti-atherosclerotic potential, but their effects in humans appear to be more complex **(Young *et al*. 2001).**

Lycopene

Lycopene, a carotenoid, possesses antioxidant and antiproliferative properties in animal and in-vitro studies on breast, prostate and lung cell lines, although anticancer activity in humans remains controversial **(Saren *et al.*, 2008).** Lycopene reduces the incidence of prostate cancer. The major dietary source of lycopene is tomatoes, with the lycopene in cooked tomatoes, tomato juice and tomato sauce included, being more bioavailable than that in raw tomatoes **(Donaldson, 2004).**

Selenium

Selenium is a trace mineral found in soil, water, vegetables (garlic, onion, grains, nuts, and soybean), sea food, meat, liver and yeast **(Willcox *et al.,* 2004).** Selenium is mostly known for its potential antioxidant properties. Selenium is a trace mineral required to forms the active site of several antioxidant enzymes including glutathione peroxidase. **(Saikat and raja, 2011).** Selenium is essential for the proper function of the immune system and is known to have antiviral properties **Mckenzie *et al.* (1998); Levander (1997).** Selenium is also necessary for the thyroid function. Selenium deficiency can occur in patients on total parenteral nutrition (TPN) and in patients with gastrointestinal disorders. In certain China areas with Selenium poor soil, people have developed a fatal cardiomyopathy called Keshan disease which was cured with Selenium supplement **(Higdon, 2007).**

Flavonoids

Sunil, (2014) reported that Flavonoids promote antioxidant activity, cellular health and normal tissue growth and renewal throughout the body. Flavonoids are polyphenolic compounds which are present in most plants. Beneficial effects of flavonoids on human health mainly reside in their potent antioxidant activity **(Miller, 1996).** They have been reported to prevent or delay a number of chronic and degenerative ailments such as cancer, cardiovascular diseases, arthritis, aging, cataract, memory loss, stroke, Alzheimer's disease, inflammation and infection. They also work with vitamin C to reduce oxidative stress for the water based portion of the cell and may slow down some of the effects of aging. There are more than 4,000 unique flavonoids and they are most effective when several types are consumed together. Food sources include: cranberries, kale, beets, berries, red and black grapes, oranges, lemons, grapefruits and green tea **(Banerjee *et al.* 1993).**

ANTIOXIDANTS TO PREVENT DESEASES

Heart Disease

High cholesterol levels, hypertension, cigarette smoking, and diabetes, are believed to promote atherosclerosis, a growing body of evidence suggests a critical step in its development is the oxidation of low-density lipoprotein (LDL) within the arterial wall **(Jialal and Fuller, 1993)**. Antioxidants have been shown to prevent LDL oxidation in-vitro and retard the progression of atherosclerosis in animal models. Several human studies found supplemental vitamin E increased the resistance of LDL oxidation, and decreased the rate of LDL oxidation. It has been estimated that dietary increases in antioxidant vitamins may reduce the risk of heart disease by 20-30% **(Hennekens and Gaziano, 1993).**

Cancer

The development of cancer in humans is a complex process including cellular and molecular changes mediated by diverse endogenous and exogenous stimuli. It is well established that oxidative DNA damage is responsible for cancer development **(Valko *et al.,* 2004).** DNA mutation is a vital step in carcinogenesis and elevated levels of oxidative DNA lesions have been noted in various tumors, strongly involving such damage in the etiology of cancer. Epidemiological evidence consistently relates low antioxidant intake or low blood levels of antioxidants with increased cancer risk **(Block *et al.,* 1992).** It is believed that antioxidants exert their protective effect by decreasing oxidative damage to DNA and by decreasing abnormal increases in cell division. Both cigarette smoking and chronic inflammation– are two of the major causes of cancer–have strong free radical components in their mechanisms of action **(Mark, 1998).** Antibiotic antioxidants like vitamin C, vitamin E and β-carotene also found to have preventive role against cancer. Antioxidant diet or consumption of antioxidant like vitamins E, vitamins C, and selenium may have potential role in enhancing the efficacy of

cancer treatment, they may also protect against side effects to normal tissues that are associated with treatment **(Saikat and Raja, 2011; Borek, 2004; Valko *et al.*, 2007).**

Pulmonary Disorders

The pathogenesis of chronic pulmonary disorders like asthma and chronic obstructive pulmonary disease (COPD) are characterized by systemic and local chronic inflammation and oxidative stress **(Caramori and Papi 2004; Guo and Ward, 2007; Lean *et al.*, 2008).** Cellular damage caused by free radicals is thought to be partly responsible for the bronchial inflammation characteristic of this disease **(Saikat and Raja 2011).** An air pollutant such as ozone and cigarette smoking, infections, and other allergens increases generation of free radicals and amplify the risk of pulmonary disorders. It has been suggested that increasing antioxidant intake may help to reduce oxidant stress and help to prevent or minimize the development of asthmatic symptoms **(Greene, 1995).** Flavanoids also reduce asthma inflammation through antioxidant, anti-allergic and anti-inflammatory properties **(Saikat and Raja 2011).** Vitamin C, vitamin E and beta carotene supplementation has been associated with improved pulmonary function **(Hatch, 1995; Bendich, 1994).** Some evidence suggests glutathione or possibly N-acetyl cysteine, which is a precursor to glutathione, may be helpful in protecting against pulmonary damage as well **(Bland, 1995).**

Cardiovascular Disease and Oxidative Stress

Oxidative stress is a primary or secondary cause of many cardiovascular diseases **(Lien *et al.*, 2008).** Cardiovascular disease is of multifactorial etiology associated with a variety of risk factors for its development including hypercholesterolemia, hypertension, smoking, diabetes, poor diet, stress and physical inactivity amongst others (**Chatterjee *et al.*, 2007**; **Ceriello., 2008).** Free radicals produced by lipid oxidation damage the walls of blood vessels and lipoproteins and other particles circulating in the blood. The best way of preventing cardiovascular disease is to increase the concentration of antioxidants in the blood to keep the concentration of free radicals at low levels. **(Freis, 1994).** Antioxidant vitamins like vitamin C, vitamin E and β-carotene and other foods like., cereals, pulses (legume), spices, dark green leafy vegetables such as kale and spinach, citrus fruits, crude palm oil, soybean oil, cod liver oil, sprouts, peppers, whole grain, honey, walnuts and black tea can significantly increase the hepatic antioxidant enzymes reduces the risk of cardiovascular diseases. Flavanone, flavanol, flavone, isoflavone, phenolic acid and anthocyanins are natural antioxidant component found in fruit and vegetables **(saikat and Raja 2011).**

Alzheimer's disease

Alzheimer's disease 4-hydroxy-2, 3-nonenal, acrolein, malondialdehyde and F2-isoprostanes are important break down products of lipid peroxidation. Elevated HNE levels have been observed in Alzheimer's disease **(Selley *et al.*, 2002; Butterfield *et al.*, 2002).** Cerebrospinal fluid of patients with Alzheimer's disDNA bases is susceptible to modification by oxidative stress involving hydroxylation **(Gabbita *at al.*, 1998).** In the Alzheimer diseased brain, the activity of the antioxidant proteins catalase, superoxide dismutase (SOD), glutathione peroxidase and glutathione reductase are increased in the hippocampus and amygdale **(Rahman *et al.*, 2012; Zemlan et al., 1989; Pappolla et al., 1992).**

Rheumatoid Arthritis

Rheumatoid arthritis is an autoimmune disease characterized by chronic inflammation of the joints and tissue around the joints with infiltration of macrophages and activated T cells. An increase in reactive oxygen species plays an important role in the pathogenesis of rheumatoid arthritis **(Lemarechal *et al.*, 2006; Rahman *et al.*, 2012).** Oxidative

damage and inflammation in various rheumatic diseases were proved by increased levels of isoprostanes and prostaglandins in serum and synovial fluid compared to controls **(Lien *et al*., 2008).** Intake of certain antioxidant micronutrients, particularly β-cryptoxanthin and supplemental zinc and possibly diets high in fruits and cruciferous vegetables, also confer protective against the development of rheumatoid arthritis **(Saikat and Raja, 2011).**

Diabetes

Oxidative stress and oxidative damage to the tissue are common end points of some chronic diseases, like diabetes **(John *et al.*, 1999).** Diabetes mellitus is associated with increased formation of free radicals and decrease in antioxidant potential. Both insulin dependent (type 1) and non-insulin-dependent diabetes (type 2) are associated with increased oxidative stress **(Valko, *et al.*, 2007; Rahimi *et al*., 2005).** Several studies are reported the depletion of antioxidant enzyme levels in patients with diabetes. Photochemical with antioxidant activity like cinnamic acids, coumarins, diterpenes, flavonoids, lignans, monoterpenes, phenylpropanoids, tannins and triterpenes also proved beneficial to protect diabetes or protect diabetic complications. **(saikat and Raja, 2011 ; Montonen, *et al*., 2004).**

Neurodegenerative Diseases

Free radical induced oxidative stress has been investigated in neurological diseases including Alzheimer's disease, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis (ALS), memory loss, depression **(Singh *et al.*, 2004).** Use of antioxidant like α-lipoate, coenzyme Q10, melatonin, phenyl-alpha-tert butyl nitrone, flavanoid, GSH-glycosid and Euk-8 (a salen-manganese complex) also produced beneficial effect in such diseases **(Saikat and Raja 2011).**

Aging

Aging in humans is associated with changes in physical characteristics and decline of many physiological functions. Increased accumulation of free radicles heightens the vulnerability of older individuals to a variety of oxidative stress. These radicals are capable of causing apoptosis, necrosis and cell death **(Irshad and Chaudhuri, 2002; Niki, 2000; Orr and Sohal 1994.)**

SUMMERY AND CONCLUSIONS

Modern civilization with the use of different chemicals, pesticides, pollutants, smoking and alcohol intake and even some of synthetic medicine increases the chance of disease due to free radicals. Antioxidants are important of an intake of dietary antioxidants when protecting against damage induced by free radicals and oxidative stress. Sources of natural antioxidants are fruit and vegetables, cereals, legumes, nuts and oilseeds. It can be conclude that intake of antioxidants in our daily diet may give good health.

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